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EXAMINER	
FISHER, ABIGAIL L	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,990	SCHACHT ET AL.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-13 and 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-13 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed on May 29 2009 is acknowledged. Claims 7 and 14 were/stand cancelled. Claims 1-6, 8-13 and 15-18 are pending.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Abstract

The objection to the abstract is **withdrawn** in light of Applicants' filing of a new abstract on 5/29/09 in which the abstract is one paragraph.

Specification

The disclosure is objected to because of the following informalities: oxybutynin (as oxybutynine) is spelled incorrectly on page 6 line 17.

Appropriate correction is required.

Response to Arguments

The rejection is maintained as applicants' have not responded to or corrected the objection to the specification set forth in the Office action mailed on 2/2/09.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claim 14 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is **withdrawn** in light of the cancellation of the claim in the reply filed on May 29 2009.

Claims 1-5, 8, 10-13 and 15-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses chemicals, such as oxybutynin, rotigotine, fesoterodine, fentanyl, aminotetralin, and silica which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claim(s) 1-5, 8, and 10-18 is(are) directed to encompass any amine functional drug, which only corresponds in some undefined way to specifically instantly disclosed chemicals. Claim 10 additionally recites that the matrix is free of particles that can absorb salts of the amine functional drug. None of these amine functional drugs or particles that can absorb salts of the amine functional drug meet the written description provision of 35 USC § 112, first

paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompass a myriad of possibilities. Applicants have provided no definition as to what constitutes an amine functional drug except indicating four specific drugs that are considered amine functional drugs. Applicants have only indicated particles that can absorb salts of the amine functional drug are silica. Additionally, claims 3 and 4 recite that the amine functional drug has an octanol/water partitioning coefficient (log p) $\geq$ 2.8 at pH 7.4 and a pKa of 7.4 to 8.4. The instant application only claims one specific drug and that is oxybutynin, however as evidenced by Quan et al. (US Patent No. 5834010, cited on PTO Form 1449), Oxybutynin has a pKa of 10.3 (example 1), which is outside of the claimed range, therefore this compound would not meet the limitations of this claim. The specification does not specifically point out any drug that would meet the limitation of instant claims 3 or 4. The specification provides insufficient written description to support the genus encompassed by the claim. **Note: MPEP 2163.**

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, (Fed. Cir. 1991), makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), further supports this by stating that:

The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or

recognize the identity of the subject matter purportedly described. (Emphasis added).

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed amine functional drugs or particles, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Circ. 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016, (Fed. Cir. 1991). In Fiddes v. Baird, 30 USPQ2d 1481, 1483, (Bd. Pat. App. & Int. 1993), claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 (Fed. Cir. 1997) held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Furthermore, to the extent that a functional description can meet the requirement for an adequate written description, it can do so only in accordance with PTO guidelines stating that the requirement can be met by disclosing "sufficiently detailed, relevant identifying characteristics," including "functional characteristics when coupled with a known or disclosed correlation between function and structure." Univ. of Rochester v. G.D. Searle, 68 USPQ2d 1424, 1432 (DC WNY 2003).

Therefore, only the above chemically structurally defined chemicals, but not the

full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Response to Arguments

Applicants argue that (1) an amine-functional drug is a drug containing a protonatable amine group and one can easily find such drugs. The instant specification discloses four drugs containing the amine functionality and therefore is representative of the genus. Furthermore, applicants argue that oxybutin is not required to meet the limitation of the dependent claims (specifically 3 and 4) and the cited art by the examiner indicates that rotigotine possess the claimed octanol/water distribution coefficient and pka. Applicants argue that (2) clearly they have support for the limitation of claim 10.

Applicants' arguments filed May 29 2008 have been fully considered but they are not persuasive.

Regarding applicants first argument, the instant claims recite a large genus which is amine-functional drug. This description is therefore any drug that possesses the functional group of an amine. The instant specification recites four specific drugs: the dopamine agonist rotigotine, the pain reliever fentanyl and anticholinergic drugs: oxybutynin and fesoterodine. If the instant claims only recited that the drugs

incorporated into the transdermal system were that of amine functional drugs that would be one thing. However, the instant claims attempt to further limit the instantly claimed amine functional drugs. Since the instant specification only describes four drugs and the examiner has shown that at least one of them does not meet the limitations of these claims, one of ordinary skill in the art would not envision which compounds applicants are attempting to claim by the recited claim language. Since the instant specification only teaches four compounds, this is the only support provided for amine functional drugs that would meet the limitations of the claims and therefore one of ordinary skill in the art would not be apprised of the scope or be able to visualize or recognize the identity of the subject matter purportedly described.

Regarding applicants second argument, since the instant specification only recites four specific amine functional drugs and the instant specification only recite one specific particle (silica), that is the only particle described which would be known to absorb the salts of the amine functional drug and the only specie which would be recognized as the subject matter of claim 10.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 10-11 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over D'Angelo et al. (US Patent No. 5932240) in view of Muller et al. (WO 99/49852, cited on PTO Form 1449) as evidenced by Nugroho et al. (Pharmaceutical Research 2004).

Applicant Claims

Applicant claims a transdermal delivery system comprising a backing layer, a self adhesive matrix containing an amine-functional drug and a protective foil or sheet to be removed prior to use wherein the self-adhesive matrix comprises a sold or semisolid semi-permeable polymer wherein an amine functional drug in its free base form is incorporated which comprises within the matrix 10^3 to 10^9 microreservoirs per cm^2 of the surface of the matrix, said microreservoirs containing the amine functional drug which is permeable to the free base of the amine functional drug which is substantially impermeable to the protonated form of the amine functional drug and wherein the microreservoirs have a maximum diameter that is less than the thickness of the matrix and is not greater than 34 micrometers and wherein the backing layer is inter to the components of the matrix.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

D'Angelo et al. (US Patent 5,932,240) teach multidose transdermal drug delivery system comprising a laminate composite with a plurality of compartments, wherein each compartment is a reservoir for a unit dose of a drug active to be transdermally administered, wherein said unit doses being in the form of a multiphase composition of microspheres wherein an internal phase comprises the drug actives and adjuvants, and said internal phase is surrounded by an outer phase of film-forming polysaccharides engrafted with transdermal promoters, said microspheres being distributed through a diffusible matrix of said composition (abstract and reference claim 1). The patch assembly consists of a base in which the steady state dosage is contained as needed

by the patient and individual medicament reservoirs which may be activated by either a "tear-and-release" or "pull-and-release" mechanism (i.e. backing layer; col. 2, lines 56-61). The reservoirs contain medicament which can be the same as contained in the base or various unit dosages of the base (col. 2, lines 61-67). D'Angelo et al. teach that various drugs can be delivered in unit doses, including antiparkisonism drugs (col.1, lines 57 to col. 2, line 21; col. 2, line 67 to col. 3, line 8). D'Angelo et al. teach a multidose transdermal drug delivery system comprising a laminate composite of a drug-permeable membrane to be placed in contact with a patient's skin; a transfer gel layer disposed on the membrane; a permeable membrane disposed on the transfer gel layer; overlaid impervious drug enclosure means for receiving and protectively enclosing a drug active to be transdermally administered; wherein the drug enclosure means and the permeable membrane defining a plurality of compartments there between defining reservoirs for respective unit doses of the drug active; and individual activation means for releasing unit doses of the drug active form respective ones of the compartments for contacting with the patient's skin (col. 3, lines 9-23). D'Angelo et al. teach reservoirs comprising microencapsulations of the drug active, wherein the drug active may be insulin encapsulated into capsules of substantially 1 to 150 microns diameter, the microencapsulations are formed of a layer of polymer encapsulating the drug active, the polymer layer having drug-penetration moieties engrafted thereon (col. 3, lines 51-57). D'Angelo et al. disclose that laminate composite forming the reservoirs for the drug actives and associated vehicles may be formed from flexible or rigid materials, including regenerated cellulose (cellophane), ABS polymer/cellulose acetate (col. 4, lines 44-56).

D'Angelo et al. teach Cotran 9872 acrylate adhesive for adhering the patch to the skin (= **self-adhesive layer**; col. 7, lines 2-9).). D'Angelo et al. teach that useful dimensions for the patch are approximately one inch by two inches and up to about one quarter to half inch in thickness (col. 4, lines 61-63), while the size of each reservoir is determined by the volume of the unit dose to be administered (col. 4, lines 63-67). D'Angelo et al. teach that the drugs and their adjuvants are dissolved, suspended, absorbed or contained in matrices or solutions, wherein useful matrices are gels of bipolymers such as alginates, gelatins, chitin, and **PVP** (col. 5, lines 2-3). The size of the microcapsules varies between 1 and 150 microns depending on the desired concentrations of the drugs to be administered (column 6, lines 19-21).

Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)

Although D'Angelo et al. al. teach that transdermal drug delivery systems wherein various drugs, such as antiparkinsonism drugs may be included in the microreservoirs, and acrylate adhesive for adhering the patch to the skin, this reference does not teach the specific instantly claimed aminotetralin compound or silicone pressure adhesive. However, this deficiency is cured by Muller et al.

Muller et al. (where US Patent No. 6884434 is serving as the English Language equivalent of WO 99/49852) is directed to a transdermal therapeutic system which contains a D2 agonist. The device is utilized for the treatment of Parkinson's syndrome (column 1, lines 9-10). The matrix systems for drug delivery in their simplest forms consists of a backing layer, an active substance containing self-adhesive matrix and a protective film to be removed prior to use (column 2, lines 51-56). The adhesive system

are either acrylate-based or silicone-based (column 2, lines 36-37). Silicone adhesives are in most cases polydimethylsiloxanes. However other organic residues may in principle be present instead of the methyl groups. The silicone adhesives are available as one component adhesives in two variants as so-called amine-resistant and as non-amine-resistant adhesives. Due to the basic nature of rotigotine (5,6,7,8-tetrahydro-6-[propyl-2[-(20thienyl)ethyl]amino-1-naphthalenol), silicone adhesives that are amine-resistant are used (column 3, lines 1-10). The adhesive's dissolving capacity of the active substance is an important parameter for the development of matrix systems (column 3, lines 15-17). It is taught that for silicone adhesives only the active substance base is suitable for use as salts thereof are practically insoluble in these types of adhesives. Additionally it is taught that if polyvinylpyrrolidone is added to the adhesive, the dissolving capacity for the free base in such matrices is increased (column 3, lines 55-67). Auxiliary substances such as alkaline substances can be added a solution of the active substance in order to convert the active substance hydrochloride into the free active substance base. Then the solution may be filtered whereby the reactants with the exception of the active substance are eliminated (column 4, lines 28-48).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al. and Muller et al. and utilize silicone adhesives. One of ordinary skill in the art would have been motivated to utilize silicone adhesives as D'Angelo et al. teach that acrylate adhesives can be utilized and Muller et al. teach that silicone adhesives or acrylate adhesives can be utilized. One of

ordinary skill in the art would have been motivated to replace acrylate adhesives with silicone adhesives as both are taught by Muller et al. as functional equivalents. One of ordinary skill in the art would have a reasonable expectation of success as both D'Angelo et al. and Muller et al. are directed to transdermal delivery devices.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al. and Muller et al. and utilize rotigotine free base in the drug delivery device. One would have been motivated to add rotigotine free base to the transdermal delivery system to provide multiple unit doses of rotigotine because D'Angelo suggest that drugs used to treat Parkinson's disease may be included in the microreservoirs of the transdermal patch and Muller et al. is directed to transdermal delivery systems comprising rotigotine which is a drug taught as treating Parkinson's disease. One of ordinary skill in the art would have been motivated to utilize the rotigotine free base when utilizing silicone adhesives as it is taught by Muller et al. that the free base or the hydrochloride salt which is converted to the free base are soluble whereas salts of the active substances are practically insoluble in these types of adhesives. Furthermore, one of ordinary skill in the art would have been motivated to incorporate rotigotine into a microreservoir transdermal delivery patch as one would appreciate the desirability of administering multiple unit doses, wherein a given dose of a drug is delivered transdermally in multiple doses instead of a single large dose, as this would allow smaller doses of the drug to be administered to a patient per unit of time, which would result in less dose-related side effects.

It is noted that D'Angelo et al. teach PVP and Muller et al. teaches that if polyvinylpyrrolidone is added to the adhesive, the dissolving capacity for the free base in such matrices is increased. Therefore, one of ordinary skill in the art would have been motivated to add PVP in order to increase the dissolving capacity the drug. One of ordinary skill in the art would have a reasonable expectation of success as D'Angelo et al. teach that PVP incorporation is suitable.

Regarding the claimed number of microreservoirs and the size of the microreservoirs, D'Angelo teaches microcapsules of a diameter of 1 to 150 microns, which vary depending on the desired concentration of the drug. Therefore, it would have been obvious to one of ordinary skill in the art to vary the number of microreservoirs or the size of the microcapsule depending on the desired amount of drug to be administered.

Regarding instant claim 10, Muller et al. teach that their invention is an improvement over WO-9407468 because WO '458 requires hydrated silicate dispersed therein for taking up the hydrophile drug salt. This results in coating products and it much more difficult to manufacture and in the system of WO '458 only the salt of the drug can be used. Muller et al. teach that their invention avoids these disadvantages (column 2, lines 5-27). Therefore, it would have been obvious to one of ordinary skill in the art to exclude silicate, which are particles that absorb salts of the amine functional drug, based on the teachings of Muller et al.

Regarding instant claims 3 and 4, as evidenced by Nugroho et al. the octanol/water distribution coefficient of rotigotine at pH 7.4 is 3.41 (page 846, last sentence) and the pKa is 7.9 (page 847, first sentence).

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over D'Angelo et al. in view of Muller et al. and in further view of Quan et al. (US Patent No. 5834010, cited on PTO Form 1449).

Applicant Claims

Applicants claim the amine functional drug is oxybutynin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of D'Angelo et al. and Muller et al. are set forth above. D'Angelo et al. is directed to a multidose transdermal drug delivery system comprising microreservoirs. Pharmacological active agents taught that can administered transdermally include Parkinsonism control agents and anti-cholinergic (columns 1-2, lines 58-67 and 1-21). Muller et al. teach utilizing silicone adhesives in transdermal patches with the free base of drugs.

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

D'Angelo et al. do not teach that the anti-cholinergic drug that can be administered is oxybutynin. However, this deficiency is cured by Quan et al.

Quan et al. is directed to the use of triacetin as a penetration enhancer for transdermal delivery of a basic drug. Drugs taught that can be delivered include oxybutynin (example 1).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al., Muller et al. and Quan et al. and utilize oxybutynin as the drug to be delivered. One of ordinary skill in the art would have been motivated to utilize oxybutynin as D'Angelo et al. teach that drugs that can be delivered transdermally include anti-cholinergic drug and Quan et al. teach that oxybutynin, which is a specific anti-cholinergic, can be delivered transdermally. Furthermore, the selection of a specific drug is considered prima facie obvious depending on the desired condition/symptoms to be treated.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over D'Angelo et al. in view of Muller et al. and in further view of Pfister et al. (US Patent No. 5232702) and as evidenced by Nugroho et al.

Applicant Claims

Applicants claim the polymer matrix comprises two or more silicone pressure sensitive adhesives. Applicants claim the silicone pressure sensitive adhesive is a blend of a high tack silicone pressure sensitive adhesive comprising polysiloxane with a resin and medium tack silicone pressure sensitive adhesive comprising polysiloxane with a resin.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of D'Angelo et al. and Muller et al. are set forth above. D'Angelo et al. is directed to a multidose transdermal drug delivery system comprising microreservoirs. Muller et al. teach utilizing silicone adhesives in transdermal patches with the free base of drugs.

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

D'Angelo et al do not teach utilizing a blend of high tack and medium tack silicone pressure sensitive adhesives. However, this deficiency is cured by Pfister et al.

Pfister et al. is directed to silicone pressure sensitive adhesive compositions for transdermal drug delivery. Example B (column 13) teach that an adhesive formulation consisting of a low silanol containing amine compatible silicone adhesive (Adhesive II) and a high silanol containing silicone adhesive (adhesive I) were prepared. The

compositions were evaluated for flow reduction and creep resistance. It is taught that adhesive II has lower cohesive strength and exhibits significantly more flow when compared to adhesive I, which in many cases this is a disadvantage where an amine compatible adhesive is required. However, by combining adhesive I and adhesive II, a significant reduction of flow and improved creep resistance was achieved.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of D'Angelo et al., Muller et al. and Pfister et al. and utilize a combination of a low silanol containing amine-compatible silicone adhesive and a high silanol containing silicone adhesive. One of ordinary skill in the art would have been motivated to utilize this combination as it is taught by Pfister et al. as providing an adhesive with significant reduction of flow and improved creep resistance where amine-compatible adhesives are required. As taught by Muller et al. when utilizing a basic drug such as rotigotine, amine-resistant adhesive are used. Therefore, one of ordinary skill in the art would have been motivated to utilize this mixture in order to provide an adhesive with significant reduction of flow and improved creep resistance.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicants argue that (1) nothing in D' Angelo would motivate one of ordinary skill to select the class of amine-functional drugs among the large list of allegedly possible pharmacological agents. D' Angelo states that almost any drug to some degree can be administered transdermally therefore the combination of D-Angelo and Mueller can only be made by hindsight reconstruction of the invention. Applicants argue that (2) there is no teaching or suggestion of microreservoirs within a self-adhesive matrix such that there is not a layer that either contains the microcapsules or lies over or under the microcapsule containing layer. Applicants argue that (3) there is no teaching or suggestion of the microreservoirs having a maximum diameter less than the thickness of the layer wherein they are embedded. Applicants argue that (4) they take issue with the Examiner's statements regarding polyvinylpyrrolidone and that these statements appear to utilize hindsight reconstruction.

Applicants' arguments filed May 29 2009 have been fully considered but they are not persuasive.

Regarding applicants first argument, the exemplified drug of D' Angelo et al. is that of insulin, which due to the nature of it being a peptide chain would necessarily be a amine-functional drug (as evidenced by Stryer pages 20-22 and 25 wherein insulin is an amino acid chain in which the first amino acids of the chain as well as the lysine, arginine and histidine would all have protonatable nitrogens). Secondly, the large list taught by D' Angelo and the statement that almost any drug can be utilized would suggest to one of ordinary skill in the art that any drug can be utilized. Since, as taught

by Mueller, rotigotine which is a Parkinson's drug which is a group taught suitable by D' Angelo, is known to be utilized for the treatment of Parkinson's Disease and to be delivered transdermally, one of ordinary skill in the art would have been motivated to utilize these specific species of amine functional drugs based on the teachings of D' Angelo et al. and Mueller. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). D' Angelo et al. suggest the incorporation of Parkinsonism drugs and Mueller teach that one such drug which is known to be delivered transdermally. Therefore, when desiring to treat Parkinson 's disease one of ordinary skill in the art would have been motivated to incorporate the specific amine-functional drug, rotigotine. Additionally, the instant claims recite the incorporation of "an amine-functional drug" this is interpreted as one amine functional drug, not the whole genus/class of amine functional drugs. Therefore, in order to anticipate/render obvious that particular limitation of the claims the cited prior art only needs to recite one amine functional drug.

Regarding applicants' second argument, firstly applicants appear to recognize that D' Angelo et al teach the incorporation of a microcapsule adhesive 19 as they refer to it on page 12 in the response. Therefore as seen from figure 2, this microcapsule

adhesive is found both above and below the microcapsules. D' Angelo teaches that the acrylate adhesives by 3M are approved for contact to the skin and are commercially offered for transdermal patch adhesive. Therefore, the adhesive defines the matrix containing the drug, which is present both below and above the encapsulated drug.

Regarding applicants' third argument, D' Angelo et al. teach microreservoirs having microencapsulations of the drug active having a diameter substantially of 1 to 150 microns. Since the self-adhesive matrix proves a means to active the reservoirs by either a tear-and release or pull and release mechanism this layer would be expected to be visible to the naked eye and therefore the microreservoirs (being of micron diameter) would be expected to have a diameter that is less than the thickness of the self-adhesive matrix.

Regarding applicants fourth argument, the examiners statement about the dissolving capacity of PVP is specifically taught by Muller et al. (column 3, lines 55-67). Since Muller et al. teaches that if polyvinylpyrrolidone (PVP) is added to the adhesive, the dissolving capacity for the free base in such matrices is increased this provides the motivation to one of ordinary skill in the art to utilize PVP because regardless the location of the adhesive, the drug at some point has to pass through the adhesive in order to be transdermally administered. Therefore, one of ordinary skill in the art would have been motivated to add PVP in order to increase the dissolving capacity the drug and thereby increasing administration. This is not hindsight construction but a specific teaching of Muller et al. While, D'Angelo et al. teach the incorporation of PVP for another purpose, PVP is still taught as a component that can be included in the

transdermal patch. Therefore, one of ordinary skill in the art would have a reasonable expectation of success.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
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